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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional)
000250.00003

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to "Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)]

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Application Number	Filed
09/853,880	May 14, 2001

First Named Inventor
Gregory J. Riggins

Art Unit	Examiner
1643	C. Yaen

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest.
See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed.
(Form PTO/SB/96)

☒ attorney or agent of record. Registration number **42,653**.

☐ attorney or agent acting under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34 _____

Signature

Lisa M. Hemmendinger
Typed or printed name

202 824-3000
Telephone number

December 12, 2005
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required.
Submit multiple forms if more than one signature is required, see below*.

☒ *Total of **1** forms are submitted.

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	Group Art Unit: 1642
Gregory J. Riggins *et al.*	)	Examiner: C. Yaen
Serial No.: 09/853,880	)	Atty. Docket No. 000250.00003
Filed: May 14, 2001	)	

For: FOUR GENETIC TUMOR MARKERS SPECIFIC FOR HUMAN GLIOBLASTOMA

REASONS SUPPORTING PRE-APPEAL BRIEF REQUEST FOR REVIEW

U.S. Patent and Trademark Office
Customer Service Window
Randolph Building
401 Dulany Street
Alexandria, VA 22314

Sir:

This paper accompanies a Pre-Appeal Brief Request for Review and a Notice of Appeal. Claims 13, 16, and 18-22 are pending and are rejected only under 35 U.S.C. § 112 ¶ 1 as not enabled. There are clear errors in this rejection.

Independent claim 13 and dependent claims 16 and 18-22 are directed to a method of specifically delivering a reagent to a glioblastoma. Claim 13 recites a step of "contacting cells of the glioblastoma with an antibody which is conjugated to a reagent, wherein the antibody specifically binds to an extracellular epitope of glycoprotein (transmembrane) nmb (GPNMB) (SEQ ID NO:17), whereby the reagent is delivered to the cell."

The rejection for lack of enablement is based on two assertions:

1. Delivering antibody-conjugated reagents to specific targets is unpredictable; and
2. The specification does not prove that GPNMB protein is up-regulated in glial tumors.

The Examiner did not properly apply controlling legal precedent or U.S. Patent and Trademark Office rules with respect to either of these two assertions.

1. Delivering antibody-conjugated reagents to specific targets

The Examiner cited two references, Curti[1] and Jain[2], to support the enablement rejection. Curti and Jain are not probative of enablement in this case. Jain does not even mention antibodies. Curti actually undermines the Examiner's assertion that targeting antibodies to tumors is unpredictable: "In general, the monoclonal antibodies studied for therapy or their use in imaging human tumors after intravenous administration will localize to the tumor . . . ." Page 35, first full paragraph. The remainder of Curti's discussion of antibodies (Section IV, pages 35-36) is related to factors that affect their distribution within a tumor. Neither that discussion nor the remainder of Curti's teachings is relevant to the claimed method.

Moreover, Curti and Jain were published 8 and 5 years, respectively, before this application's May 14, 2001 priority date. By the time this application was filed, targeted antibody therapeutics were reliable enough to be marketed commercially. Applicants last response provided several examples:

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[1] Curti, *Clinical Review in Oncology/Hematology 14*, 29-39, 1993

[2] Jain, *Science 271*, 1079-80, 1996.

- Rituxan™, a chimeric antibody directed against CD20, was approved for treating non-Hodgkin's lymphoma in 1997; [3]
- Herceptin™, an antibody which targets the HER2 protein, was approved for treating breast cancer in 1998; [4]
- Mylotarg™, an antibody linked to a chemotherapeutic drug, was approved for treating acute myeloid leukemia in 2000; [5] and
- Campath™, a humanized monoclonal antibody which targets CD52, was approved for treating B-cell chronic lymphocytic leukemia, was launched as a commercial product in May 2001. [6]

In fact, the Examiner acknowledged that "the art does teach many methods of delivering reagents conjugated to antibodies to specific targets."[7]

To make a *prima facie* case of non-enablement the Examiner must weigh all the evidence of record. M.P.E.P. § 2164.05(a). Instead, the Examiner dismissed Applicants' probative evidence and relied solely on Curi and Jain, which are not probative of enablement. This was clear error.

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[3] Tab E of the response filed March 17, 2005.

[4] Tab B of the response filed March 17, 2005.

[5] Tab A of the response filed March 17, 2005.

[6] Tab C of the response filed March 17, 2005.

[7] Office Action mailed December 15, 2004 at page 4 ¶ 1.

2. GPNMB protein up-regulation in glioblastoma cells

The specification teaches differential expression of GPNMB mRNA in glioblastoma cells compared to normal controls. *See, e.g.*, Figure 2. The specification teaches that "[a] reagent may be delivered to a glioblastoma using an antibody which specifically binds to an extracellular epitope of ABCC3 or GPNMB" using, preferably, an antibody which "is specific for an extracellular epitope of ABCC3 or GPNMB present at higher levels on glioblastoma cells relative to normal cells."[8] The Examiner disputes the accuracy of this statement. The Examiner contends that the record of this application provides no evidence that GPNMB protein is differentially expressed in glioblastoma cells versus normal and that therefore one skilled in the art would need to experiment in order to use a GPNMB antibody therapeutically.[9]

To demonstrate the accuracy of the specification's teaching, Applicants provided a manuscript of Kuan.[10] The Kuan manuscript demonstrated that GPNMB protein is up-regulated in glioblastomas. See Figures 6 and 7 of Kuan and Applicants' response filed March 17, 2005.

The Examiner dismissed Kuan as evidence because it is a post-filing date reference. Citing *In re Gunn* and *In re Budnick* the Examiner stated that "[p]ublications dated after the filing date providing information publicly first disclosed after the filing date generally cannot be used to show what was known at the time of filing."[11] *Gunn* and *Budnick* are inapt. Applicants did not cite Kuan to provide information not available at the filing date; the information at issue here was provided in Applicants' specification. Rather, Applicants provided Kuan to rebut the Examiner's assertion that a teaching in the specification is inaccurate. Post-filing date evidence

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[8] Paragraph bridging pages 8 and 9.

[9] Paragraph bridging pages 4 and 5 of the Office Action mailed December 15, 2004.

[10] Kuan *et al.*, "GPNMB: A Molecular Target For Human High-Grade Glioma Immunotherapy."

[11] Paragraph bridging pages 2 and 3 of the Office Action mailed July 11, 2005.

clearly is permitted for this purpose. *See, e.g., In re Marzocchi*, 439 F.2d 220, 223 n. 4, 134 U.S.P.Q. 367, 370 n.4 (C.C.P.A. 1965); *In re Hogan and Banks,* 559 F.2d 595, 605, 194 U.S.P.Q. 527, 537 (C.C.P.A. 1977); M.P.E.P. § 2124. The Examiner's refusal to consider Kuan was clear error.

Respectfully submitted,

BANNER & WITCOFF, LTD.

Dated: December 12, 2005

By: _____
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